Clinical Pharmacology Executive Summary of Aldara for MC:

In this application, 3M submitted an efficacy supplement for the indication of Molluscum Contagiosum (MC) to the above referenced NDA. NDA 20-723 was originally approved for the treatment of external genital and perianal warts on February 27, 1997 by the Division of Antiviral Drug Products. Subsequently it was approved for actinic keratosis (AK) and superficial basal cell carcinoma (sBCC) in adults by the Division of Dermal and Dental Drug Products. This is the first submission geared towards approval of Aldara™ Cream, 5% in the pediatric population.

The goal of this efficacy supplement was to obtain safety and efficacy data for the treatment of Molluscum Contagiosum (MC) in children. In this regard, the FDA provided a Written Request to 3M, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act, requesting the evaluation of imiquimod for the treatment of MC in children aged 2 to 12 years. The Written Request outlined 3 studies: 2 phase 3 studies and 1 phase 1 PK study. In this phase I study, a component of the safety assessment included measurement of PK properties of imiquimod in children. This PK study evaluated the systemic exposure of imiquimod in children under maximal use conditions. Subjects who weighed ≤25 kg applied 1 to 2 packets per dose and subjects who weighed >25 kg applied 1 to 3 packets per dose. To address the safety concern regarding the potential systemic exposure of children to imiquimod, the PK profile of imiquimod was measured under maximal usage condition predefined by the FDA.

The applicant adequately characterized the pharmacokinetics of imiquimod following single and multiple topical application in pediatric patients with MC. The systemic exposure data demonstrated that the extent of absorption of imiquimod following topical application to the MC lesional skin of the pediatric subjects was low and comparable to that observed in healthy adults and adults with AK and sBCC.

No safety concern with respect to systemic exposure of imiquimod and/or its metabolites was noted. However, the sponsor failed to demonstrate efficacy of the Aldara™ Cream, 5% in pediatric patients with MC.

Efficacy and Safety Findings:

The two phase 3 randomized, vehicle-controlled, double-blind trials involved 702 pediatric patients with molluscum contagiosum (470 exposed to Aldara; median age 5 years, range 2-12 years). In both studies, 24% of Aldara treated patients experienced complete clearance compared with 26% and 18% in Vehicle-treated patients, in studies 1494 and 1495, respectively. According to the sponsor and the clinical reviewer, neither of the phase 3 clinical studies demonstrated efficacy of Aldara for the treatment of MC. The response rate was slightly higher in the vehicle-treated arms in both studies compared with the Aldara group. In conclusion, Efficacy was not established in these studies.

According to the clinical reviewer, no deaths, SAEs, or other significant AEs were reported during the study. Local skin reactions were generally more intense at the end of

the 4-week treatment period compared with baseline. A decrease in WBC, absolute neutrophil, and absolute lymphocyte counts as well as a decrease in the percentage of neutrophils composing the WBC differential was observed in some subjects following treatment with imiquimod. According to the sponsor, none of these changes were considered clinically relevant.

1.1 Recommendation

Based on the data submitted in NDA 20-723 (S020), the application is acceptable from a clinical pharmacology perspective.

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